REMARKS

Reconsideration and allowance are respectfully requested.

Claims 2-26 are pending. The amendments are fully supported by the original disclosure and, thus, no new matter is added by their entry. Claim 25 replaces claim 1. It is a sub-genus of the general formula in the original independent claim. Claim 26 supplements claim 5.

35 U.S.C. 112 – Definiteness

Claims 1-24 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicants traverse.

The recitation "B = 0" indicate that the presence of B in the linker joining the triazine rings is optional. When B = 0, the B group is absent and the linker is comprised of an A group only. Similarly, the phrase "not necessarily equal to" simply clarifies that the substituent groups may not be the same because they have similar definitions. Similarly, the index numbers are not necessarily equal to each other because the indicated alkyl chains do not have to be the same length. Both "formulas" and "formulae" are acceptable plural forms of formula.

Claim 5 is amended and supplemented with claim 26, both reciting "and" as conjunction.

Applicants disagree with the allegation that the attributes recited in claims 6-8 do not further limit the claimed compounds and are not entitled to weight in determining patentability. As noted by the Examiner, these properties are inherent in the structure of a compound. But it is not intended that the scope of claim 1 be limited to only those compounds that can bind to anti-bodies. Instead, the scope of claim 1 defined therein by the formula and the other limitations on its chemical structure that are recited therein. All of the compounds in accordance with claim 1 do not necessarily bind to antibodies. For example, as clearly explained in the specification, the mechanism of treating disease by the compounds may not involve elimination of immune complexes.

Claim 9 is definite in reciting "at least one" as an indication that the composition may also have other active ingredients. See claims 11 to 15 for other therapeutic agents that may be included with the compounds of the claimed invention. It is also possible that the composition

may include two or more different compounds according to claim 1. None of these possibilities renders claim 9 indefinite.

Claims 21 and 24 are amended to recite how their methods are practiced. Thus, the intended scope of the claims is clear.

Applicants request withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 16-20 were rejected under Section 112, first paragraph, because it was alleged that the specification "does not reasonably provide enablement for any or all autoimmune diseases or TNF-α mediated disorders/diseases." Applicants traverse because claims 16-20 are directed to treatment of rheumatoid arthritis, which the Examiner finds enabled by the specification.

It is respectfully disputed that the claims as originally filed are "reach through" claims. The pathogenesis of autoimmune diseases and TNF-α mediated disorders/diseases is based on fundamental inflammatory processes. Applicants teach and provide adequate support in their specification that the claimed compounds can at least reduce or otherwise ameliorate tissue injury associated with an immune response to body constituents by removing free antibodies and/or antibody-antigen immune complexes from the circulation (see from page 29, line 27, to page 30, line 4). In vitro results in Examples 55 to 59 show the effects of several compounds on immune cell function. In vivo results in Examples 60 to 63 demonstrate the therapeutic effects of several compounds on systemic lupus erythematosus (SLE)-glomerulnephritis, delayed-type hypersensitivity (DTH is an animal model of psoriasis), and arthritis. These results correlate with

compounds' usefulness in treating inflammation. Thus, in animal models of human disease, the claimed compounds efficacy in treating glomerulonephritis, psoriasis, rheumatoid arthritis, or systemic lupus erythematosus in vivo was shown in working examples.

Applicants request withdrawal of the Section 112, first paragraph, rejection because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

35 U.S.C. 101 –Utility

Claims 21 and 24 were rejected under Section 101 because "the claimed recitation of use, without setting forth any steps involved in the process" is allegedly an improper definition of a process. Applicants traverse because claims 21 and 24 recite how their methods are practiced.

Withdrawal of the Section 101 rejection is requested.

35 U.S.C. 102 – Novelty

A claim is anticipated only if each and every limitation as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is claimed. See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claims 1-4 and 6-8 were rejected under Section 102(b) as allegedly anticipated by Lowik et al. (WO 01/42228). Applicants traverse.

Lowik discloses the use of larger, triazine-based, macrocyclic molecules which can bind small chemical compounds. Its disclosure is clearly distinct from the claimed invention since the compounds are structurally different larger cyclic structures and have binding preferences for different types of ligands. In particular:

a) The compounds described by Lowik contain three to six triazine members, while the claimed compound contain two triazine members.

b) The compounds described by Lowik must have at least three triazine members in order to make a cyclic structure (i.e., a macrocyclic structure). Lowik's compounds cannot bind

ligands without making a macrocyclic structure. This teaches away from the claimed invention in which Applicants teach that the claimed dimeric compounds, which cannot cyclize, may bind antibodies using only two triazine members. One of ordinary skill in the art would not have modified Lowik's disclosure to reduce the number of triazine members in the macrocyclic structure.

c) The compounds described by Lowik can bind diverse structures. Exemplification is provided for unrelated compounds: cyanuric acid and octyl glycosides. Further, Lowik discloses that macrocyclic compounds can bind a "chemical, biological or therapeutic compound" (claim 9) or, indeed, any "solute in a solution" (claim 8). In contrast, the claimed compounds may only be required to bind to the tail portion (Fc) of an antibody (a property that Lowik's compounds appear to lack), and certainly not small compounds.

In view of the above facts, there is no teaching or suggestion that would lead from Lowik's large, macrocyclic molecules with three or more triazine rings to the design of noncyclic, dimeric, triazine-based compounds which will efficiently bind antibodies. Additionally, piperazine and xylenediamine linkers are outside of the scope of the claims as amended. Finally, for Lowik's construction of macrocyclic compounds, symmetric linkers must be used. But Applicants' claimed compounds do not require symmetric linkers for their synthesis (e.g. preferred is an aminophenethyl amine linker, see claim 3).

Claim 1 was rejected under Section 102(b) as allegedly anticipated by Atkinson et al. (GB 2 053 926). Applicants traverse.

Atkinson discloses the use of an immobilized, triazine-containing dye for the purification of albumin from blood. This disclosure is also clearly distinct from the claimed invention since it requires a solid support attached to a structurally unrelated triazine dye to bind albumin, a protein which is also structurally unrelated to the preferred ligand of the claimed compounds (i.e., antibody). Moreover, the claimed compounds can bind antibody in solution. Immobilization on a solid support is not required. No biological application is taught or suggested for Atkinson's dyes in solution. In contrast, the claimed compounds can be therapeutically effective in solution. Therefore, Atkinson's disclosure teaches away from the claimed invention because the former requires attachment to a solid phase to be useful while Applicants' claimed compounds are

therapeutically effective without immobilization to an insoluble support. It is not even clear that there would be a reasonable expectation of success to modify the affinity dyes into Applicants' claimed compounds without destroying the utility of Atkinson's compounds to purify albumin.

Claims 1-4 and 6-8 were rejected under Section 102(b) as allegedly anticipated by Dore et al. (GB 2 149 808). Applicants traverse.

Dore discloses the use of unrelated triazine-containing diazo dyes and metal complexes thereof to impart colors (red and blue) on polymers such as cellulose. No biological application is taught or suggested by Dore. Although Dore's diazo dyes contain a triazine ring, they are not even remotely related to the claimed compounds in their chemical structure or biological activity. It is not even clear that there would be a reasonable expectation of success to modify the diazo dyes into Applicants' claimed compounds without destroying the utility of Dore's compounds for coloring polymers.

Claims 1-4 and 6-8 were rejected under Section 102(b) as allegedly anticipated by Adam et al. (EP 0 122 458). Applicants traverse.

Adam discloses the use of unrelated triazine-containing azo dyes for coloring/printing polymeric surfaces, such as paper. No biological application is taught or suggested by Adam. Although Adam's azo dyes contain a triazine ring, they are not even remotely related to the claimed compounds in their chemical structure or biological activity. It is not even clear that there would be a reasonable expectation of success to modify the azo dyes into Applicants' claimed compounds without destroying the utility of Adam's compounds for coloring/printing.

Claims 1-4 and 6-8 were rejected under Section 102(b) as allegedly anticipated by Cipolli et al. (EP 0 542 374). Applicants traverse.

Cipolli discloses so-called aminoplastic resins prepared by the chemical condensation of triazine-containing compounds with formaldehyde (preferred) or other aldehydes. No biological application is taught or suggested by Cipolli. Although Cipolli's resins contain a triazine ring, they are not even remotely related to the claimed compounds in their chemical structure or biological activity. It is not even clear that there would be a reasonable expectation of success to modify the resins into Applicants' claimed compounds without destroying the utility of Cipolli's compounds.

Claims 1-4 and 6-8 were rejected under Section 102(b) as allegedly anticipated by Lawery et al. (US 6,482,255). Applicants traverse.

Lawery discloses the use of unrelated triazine-containing diazo dyes as components for ink. No biological application is taught or suggested by Lawery. Although Lawery's diazo dyes contain a triazine ring, they are not even remotely related to the claimed compounds in their chemical structure or biological activity. It is not even clear that there would be a reasonable expectation of success to modify the diazo dyes into Applicants' claimed compounds without destroying the utility of Lawery's compounds as an ink.

Applicants request withdrawal of the Section 102 rejections because the cited documents fail to disclose all limitations of the claimed invention.

35 U.S.C. 103 – Nonobviousness

To establish a case of prima facie obviousness, all of the claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03. A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See id. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See id. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). Thus, a prima facie case of obviousness under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of obviousness is correct." *Kahn*, 78 USPQ2d at 1335; see *KSR*, 82 USPQ2d at 1396. An inquiry should be made as to "whether the improvement is more than the predictable use of prior art elements according to their established functions." Id. at 1396. But a claim which is

directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." Id. at 1396. Finally, a determination of prima facie obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

Claims 1-8 and 22-23 were rejected under Section 103(a) as allegedly unpatentable over Dore et al. (GB 2 149 808), Adam et al. (EP 0 122 458), Cipolli et al. (EP 0 542 374), or Lawery et al. (US 6,482,255) in view of Lowik et al. (WO 01/42228) and Atkinson et al. (GB 2 053 926). Applicants traverse because, for the reasons discussed above as regards each of the documents, they do not render obvious the claimed invention to one of ordinary skill in the art. One of ordinark skill in the art would not have had a reason to combine and modify the cited documents' disclosure to render obvious the compounds claimed by Applicants.

Applicants request withdrawal of the Section 103 rejection because the claimed invention is patentable over the cited prior art documents.

Conclusion

Having fully responded to the pending Office Action, Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

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